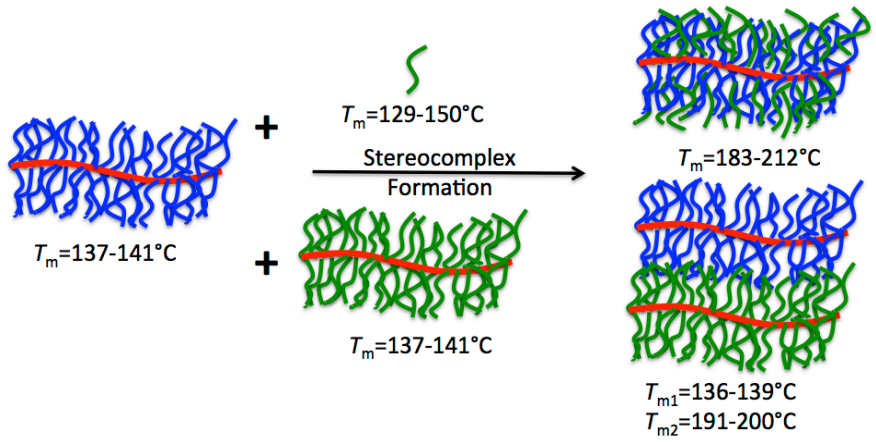
C h a p t e r 5

STEREOCOMPLEXATION OF BRUSH POLYMERS

Reproduced with permission from:
Sveinbjörnsson, B. R.; Miyake, G. M.; El-Batta, A.; Grubbs, R. H. *ACS Macro Letters* **2014**, *3*, 26-29.

ABSTRACT

In this chapter, we explore the capability of macromolecules to interdigitate into densely grafted molecular brush copolymers. We demonstrate that by using the tendency for stereocomplexation between poly(L-lactide) and poly(D-lactide) as a driving force, complementary linear polymers and brush copolymers can form a stereocomplex. However, stereocomplex formation between complementary brush copolymers is restricted, and only partially observed when the side chains are of a critical molecular weight.



INTRODUCTION

As discussed before, one of the advantages of using the self-assembly of brush polymers for applications, such as for photonic material, is that these polymers undergo very rapid self-assembly compared to the linear analogs. This is in part due to the reduced degree of entanglement for brush polymers compared to their linear analogs, as well as because of their rigid structure. Previous studies, using racemic densely grafted brush polymers with racemic poly(lactic acid) side chains, verified that neither the side chains nor the whole polymer showed evidence of entanglement.[1] Furthermore, due to the high density of the grafted polymers, densely grafted brush polymers restrict diffusion of polymers to their backbone while being permeable for small molecules.[2] To the best of our knowledge, this resistance to allowing macromolecules to diffuse through them has only been studied when there was not a strong driving force for the polymer to interact with the brush polymer side chains.

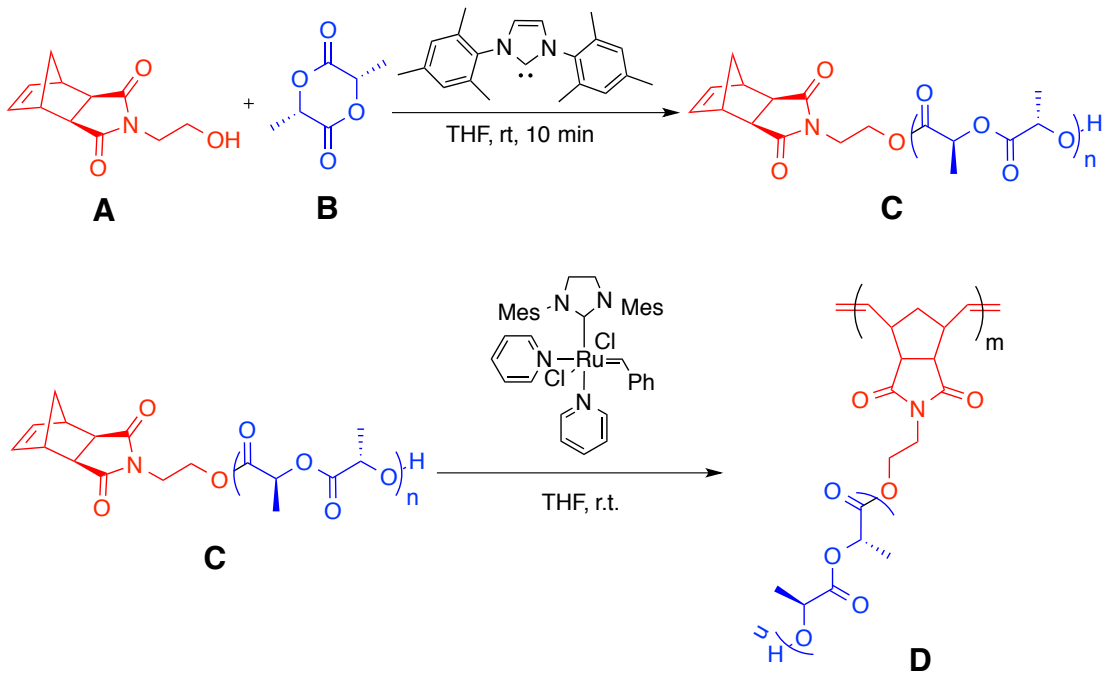
The stereoisomers poly-L-lactide (PLLA) and poly-D-lactide (PDLA) have been reported to show a strong tendency to interact with each other to form stereocomplexes,[3,4] even with certain topological restraints such as in cyclic polymers.[5] Stereocomplexes made from polylactides have a variety of uses, including biodegradable films,[6] fibers,[7,8] hydrogels,[9,10] and as nucleation agents.[11,12] Sparsely grafted polymers have also shown stereocomplex formation,[13] as well as graft polymers with oligomeric side chains.[14] This chapter describes our investigation on whether the propensity for stereocomplexation between PLLA and PDLA could act as an adequately strong driving force to allow macromolecules, both linear and brush, to diffuse through densely grafted brush side chains of various sizes to form the stereocomplexes.

RESULTS AND DISCUSSION

We utilized the macromonomer (MM) approach for the synthesis of the brush polymers, which ensures quantitative grafting density.[15–18] The MMs, PLLA, and PDLA were synthesized through modified literature procedures by ring-opening polymerization from a norbornene-based alcohol initiator catalyzed by a N-heterocyclic carbene (**Scheme 5-1**).[5,19,20] In order to study the side-chain size effect on stereocomplex formation, four pairs of PLLA and PDLA MMs were synthesized, with molecular weights ranging from 5.9-17.4 × 10^3 g/mol (**Table 5-1**). Brush copolymers were subsequently synthesized from each of the MMs via ring-opening metathesis polymerization (ROMP) using a Ruthenium-based third generation initiator (**Scheme 5-1**). The brush polymers

were synthesized with a degree of polymerization through the main chain from 100-200 MM units, yielding brush copolymers with molecular weights ranging from 1.07-2.55 × 10^6 g/mol (**Table 5-1**).

Organocatalyzed polymerization of the enantiomeric lactide monomers produces polylactide MMs that are highly isotactic.[5,21,22] The brush copolymers derived from these MMs exhibit similar optical rotations as their respective MMs, while showing consistently lower melting temperatures and heats of melting than their corresponding MMs (**Table 5-1**). In fact, differential scanning calorimetry (DSC) analysis did not reveal a melting transition temperature for the brush polymers with the shortest side chains. We attribute this to the confinement of the side chains by the brush copolymer architecture, which inhibits their mobility and capability for crystallization.



Scheme 5-1. General reaction scheme for the synthesis of the macromonomers (**C**) from a norbornene initiator (**A**) and lactide (**B**) (top) and for the synthesis of the brush copolymer (**D**) form the macromonomer (**C**) (bottom).

Table 5-1. Results for the Macromonomers and Brush Copolymers.

Sample	M_n (10^3 g/mol)[a]	PDI[b]	(Yield)/Conversion (%)[b]	[α][c]	T_m (°C)[d]	ΔH_m (J/g)[d]
L_{MM}-1	5.9	1.18	(63)	-133	129	16
L_{MM}-2	8.6	1.16	(72)	-140	148	34
L_{MM}-3	11.7	1.24	(46)	-140	150	31
L_{MM}-4	13.0	1.11	(63)	-132	144	42
D_{MM}-1	6.6	1.17	(49)	+126	128	20
D_{MM}-2	8.6	1.15	(82)	+142	149	36
D_{MM}-3	10.6	1.08	(63)	+139	149	32
D_{MM}-4	17.4	1.05	(27)	+153	149	43
L_{Br}-1	1.07 10^3	1.02	100	-139	-	-
L_{Br}-2	1.22 10^3	1.06	91	-146	139	24
L_{Br}-3	1.53 10^3	1.03	92	-147	141	13
L_{Br}-4	2.15 10^3	1.05	77	-135	137	14
D_{Br}-1	1.19 10^3	1.03	100	+121	-	-
D_{Br}-2	1.18 10^3	1.04	94	+143	138	23
D_{Br}-3	1.07 10^3	1.16	89	+140	139	25
D_{Br}-4	2.55 10^3	1.03	78	+156	139	18

[a] Measured by NMR for MMs and GPC for brush polymers. [b] M_w/M_n as measured by GPC. [c] Measured with a polarimeter (c = 3 mg/mL, $CHCl_3$). [d] Measured by DSC.

Blends of the MMs were formed by pairing similar molecular weight stereoisomers in equal weight ratios. The mixtures were dissolved in dichloromethane and stereocomplexation was achieved via controlled evaporation. Blends of the MMs with their complementary brush polymer, as well as blends of brush/brush copolymers, were prepared in an analogous manner (**Table 5-2**). After annealing, the samples were dried under vacuum and analyzed by DSC.

As expected, the MM blends (**A1-A4**) formed distinct stereocomplexes, as evidenced by the DSC analysis that showed higher melting temperatures (192-213°C) and heats of melting (37-46 J/g) (**Table 5-2**) than their pristine counterparts. The MM/brush copolymer blends (**B1-B8**) also formed distinct stereocomplexes with similar melting temperatures as the corresponding MM blends, albeit with lower heats of melting. Therefore, we infer that the MMs are able to sufficiently diffuse into the brush copolymer in order to interact with the side chains to form a stereocomplex. Interestingly, although the highest molecular weight MM/brush blends (**B4, B8**) showed stereocomplex formation, they also showed a smaller peak corresponding to the non-stereocomplexed polylactides, suggesting non-quantitative stereocomplex formation.

Table 5-2. DSC Results for the Polymer Blends.

Blend	PLLA	PDLA	T_m (°C) [a]	ΔH_m (J/g) [a]
A1	L_{MM}-1	D_{MM}-1	192	37
A2	L_{MM}-2	D_{MM}-2	212	46
A3	L_{MM}-3	D_{MM}-3	213	39
A4	L_{MM}-4	D_{MM}-4	202	43
B1	L_{MM}-1	D_{Br}-1	183	25
B2	L_{MM}-2	D_{Br}-2	211	31
B3	L_{MM}-3	D_{Br}-3	212	27
B4	L_{MM}-4	D_{Br}-4	205, 141	24, 1.9
B5	L_{Br}-1	D_{MM}-1	192	29
B6	L_{Br}-2	D_{MM}-2	210	27
B7	L_{Br}-3	D_{MM}-3	212	17
B8	L_{Br}-4	D_{MM}-4	204, 143	21, 5.8
C1	L_{Br}-1	D_{Br}-1	-	-
C2	L_{Br}-2	D_{Br}-2	137	4.3
C3	L_{Br}-3	D_{Br}-3	138	6.0
C4	L_{Br}-4	D_{Br}-4	139, 192	12, 6.5
D1 [b]	L_{Br}-2	D_{Br}-2	136, 200	18, 5.1
D2 [b]	L_{Br}-3	D_{Br}-3	136, 196	18, 5.9
D3 [b]	L_{Br}-4	D_{Br}-4	138, 191	23, 5.5

[a] Measured by DSC. [b] Blends heated at 150°C for 4 days after controlled evaporation.

The brush/brush polymer blends (**C1-C4**) showed varied properties. The blend with the shortest side chains (**C1**) did not show any transition peak in its DSC traces, like its parent brush polymers, while the two brush blends with the intermediate length side chains (**C2-C3**), showed melting temperatures close to their parent brushes but with lower heats of melting. The brush blend with the longest side chains (**C4**) showed two transition peaks, corresponding to a major melting transition temperature (138.5°C), and a weaker melting transition temperature at 191.8°C, indicative of some stereocomplex formation. We believe that longer side chains provide more conformational freedom, as the longer side-chains can extend further from the sterically congested core brush off the main chain (**Figure 5-1a**). This may allow for some interaction between brush copolymers at the chain end of the side chains, enabling some stereocomplex formation (**Figure 5-1b**). As previously noted, the brush polymers tend to have lower melting transition temperature than their corresponding MMs or blends involving MMs (both MM/MM and MM/brush blends). This leads us to conjecture that this is a result from true brush/brush interactions.

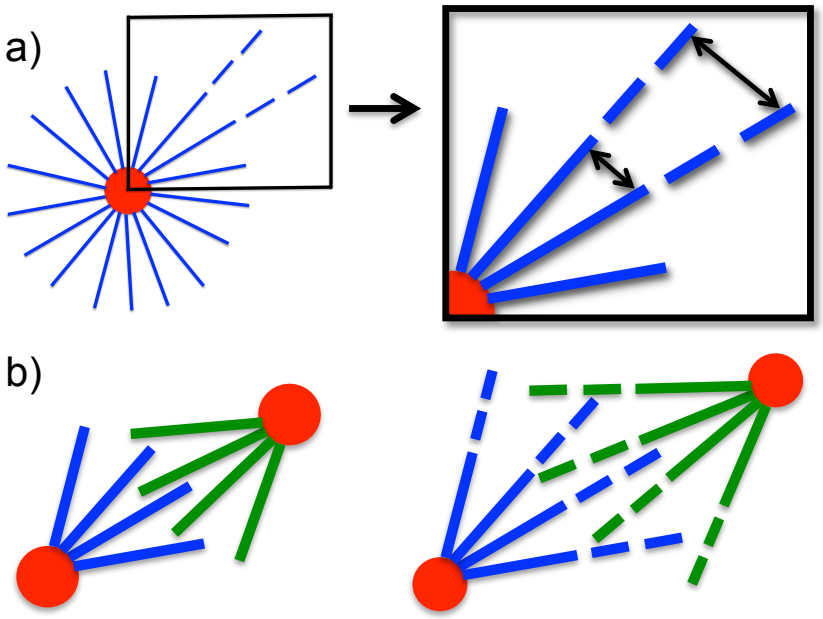


Figure 5-1. Schematics showing that a) longer side chains (where dashed lines represent extended side chain lengths) will have more conformational freedom further from the brush copolymer core, which can result in b) a potentially bigger overlap of side chains to enable stereocomplex formation

To investigate if we could thermally induce stereocomplexation, we thermally annealed the three biggest blendsunder vacuum at 150°C for 4 days after controlled evaporation (**D1-D3**, **Table 5-2**). The sample with the longest side chain (**D3**) did not show an increase in stereocomplexation, but instead the ratio between the heats of melting from before and after thermal annealing became skewed towards the non-stereocomplexed transition temperature. Meanwhile, the other two samples (**D1-D2**) started revealing evidence of some stereocomplex formation. This suggests that with heating, the benefit of the stereocomplex forming interactions can overcome the tendency of these brush copolymers to evade entangling, although only to a limited extent.

A brush statistical copolymer sample was also synthesized via ROMP by polymerizing a mixture of the lowest molecular weight MM pairs, yielding a polymer with M_n of 4.87 × 10^5 g/mol (PDI = 1.09). This polymer exhibited a melting transition temperature (175.8°C) and heat of melting (12 J/g) that suggested a weak stereocomplex formation, while the analogous brush/brush blend (C1) had not shown any stereocomplex formation. Since the other brush/brush blends did not show much stereocomplex formation either, we hypothesize that the intramolecular interactions between the PLLA and PDLA side chains in the brush statistcial copolymer must play an important role in the stereocomplex properties of the brush statistical copolymer sample.

CONCLUSION

In conclusion, we have shown that when there is an adequately strong driving force, brush polymers can allow for diffusion of macromolecules into their side chains, and we have found that at sufficient distance from the brush polymer main chain, some entanglement may begin to take place at the edges of the side chains. These results add to the intriguing properties of brush polymers and may aid in extending the scope of applications for these macromolecules.

SUPPORTING INFORMATION

Materials

$(H_2IMes)(pyr)_2(Cl)_2RuCHPh$[23] and *N*-(hydroxyethanyl)-*cis*-5-norbornene-*exo*-2,3-di-carboximide,[24] were prepared as described previously. All solvents were purchased from VWR or Sigma-Aldrich. Ruthenium-based metathesis catalyst was obtained from Materia Inc. and stored in a drybox. D(+)-Lactide was obtained from BOC Sciences, while other chemicals were bought from Sigma-Aldrich. Dry solvents were purified by passing them through solvent purification columns. Lactide monomers were purified by sublimation under vacuum. All other solvents and chemicals were used without further purification unless otherwise stated.

General Information

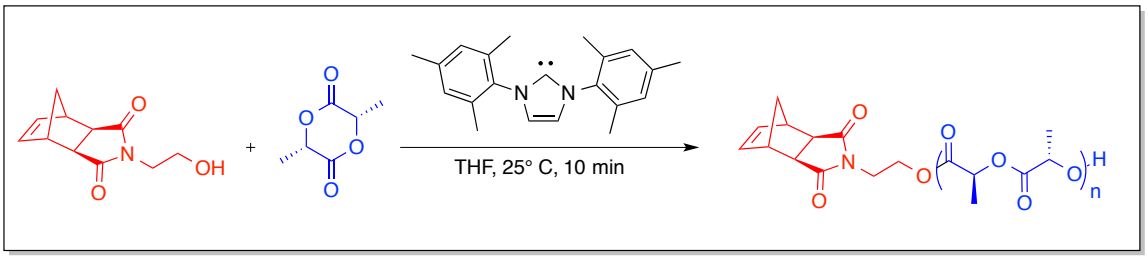
^{1}H NMR spectra were recorded at room temperature on a Varian Inova 500 (at 500 MHz). The NMR spectra were analyzed on MestReNova software and are reported relative to CDCl3 (δ 7.26). NMR abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, dt = doublet of triplets.

Gel permeation chromatography (GPC) was carried out in THF on two Plgel 10 μm mixed-B LS columns (Polymer Laboratories) connected in series with a miniDAWN TREOS multiangle laser light scattering (MALLS) detector, a ViscoStar viscometer, and Optilab rex differential refractometer (all from Wyatt Technology). The dn/dc values used for the poly(lactide) macromonomers were 0.050.

Differential Scanning Calorimetry (DSC) was performed on a Perkin-Elmer DSC 7. Samples were heated to 125°C at 20°C/min, held at 25°C for 5 minutes, and then cooled to 20°C at 10°C/min. The temperature was held at 20°C for 5 minutes before being reheated to 250°C at 10°C to determine the melting transition temperature. Finally, the samples were cooled back to room temperature at 20°C/min.

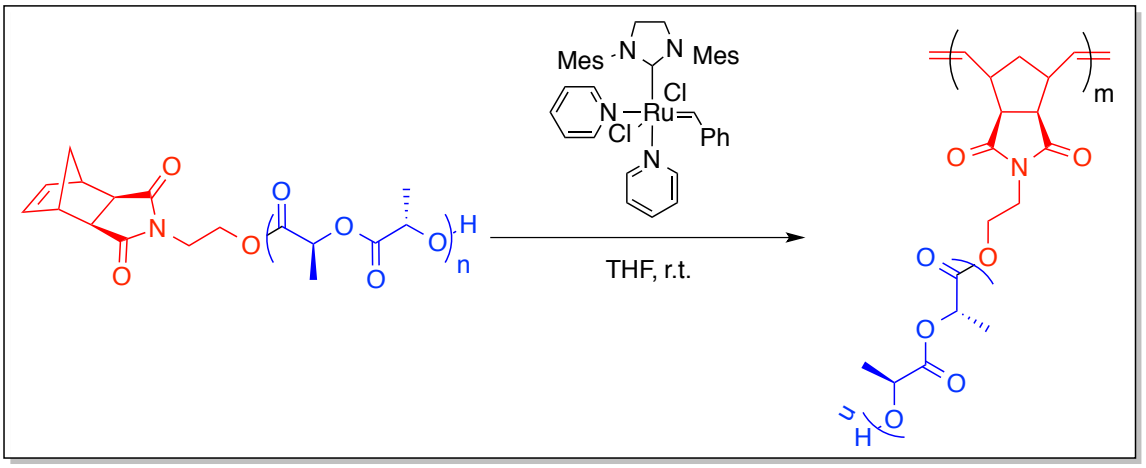
Optical rotations were measured in a solution of chloroform with a Jasco P-2000 polarimeter operating on a sodium D-line (589 nm) at 25°C, using a 10 cm path-length cell.

Synthesis



Representative procedure for the synthesis of Norbornene-Poly(lactide) (**L_{MM}-4**)

The monomer, L-Lactide (2.00 g, 13.9 mmol) was added to a 40 mL scintillation vial and dissolved in 15 mL of dry THF. The initiator, N-(hydroxyethanyl)-cis-5-norbornene-exo-2,3-di-carboximide (35.7 mg, 0.172 mmol, 1 equiv) and the catalyst, 1,3-dimesitylimidazol-2-ylidene (9.6 mg, 31.5 μmol) were added to a separate vial and dissolved in 3 mL of dry THF. Then the initiator/catalyst solution was added rapidly to the monomer solution and the whole solution allowed to stir for 10 minutes before being precipitated into MeOH. 1H NMR (500 MHz, CDCl3): δ (ppm) 6.29 (br t, 2H), 5.32-5.00 (m, 177 H), 4.40-4.24 (m, 3H), 3.83-3.69 (m, 2H), 3.27 (s, 2H), 2.70 (br q, 2H), 1.73-1.39 (m, 532H), 1.25-1.23 (m, 1H). M_n (NMR) = 13.0 kg/mol. GPC: M_n = 12.4 kg/mol, M_w/M_n = 1.11.



Representative procedure for the synthesis of a poly(lactide) brush copolymers (**L_{Br}-4**)

The poly(lactide) macromonomer (157.8 mg, 12.1 μmol) was weighed into a vial. The catalyst (2.8 mg, 3.85 μmol) was added to a separate vial. The vials were brought into the drybox and the poly(lactide) macromonomer was dissolved in THF (500 μL), while the catalyst was dissolved in

1.00 mL of THF. The catalyst solution (21 μL, 0.081 μmol) was injected via a microsyringe to the solution of macromonomers and the solution allowed to stir for 2 hours. The reaction was moved out of the dry box, quenched with butyl vinyl ether and isolated by precipitation into MeOH. GPC: M_n = 2.15 x 10^6 g/mol, M_w/M_n = 1.05.

General procedure for preparation of blends:

Equal amounts (w/w) of the complementary polymers (≈20 mg of each) were added to a small vial and subsequently dissolved in dichloromethane (≈2 mL). This solution was allowed to evaporate in the vial at room temperature, and after drying under air, it was put under high vacuum to ensure removal of the solvent.

Supplementary Tables

Table 5-3. GPC results for the macromonomers.

Sample	M_n (10^3 g/mol)	PDI
L_{MM}-1	8.16	1.18
L_{MM}-2	10.6	1.16
L_{MM}-3	14.9	1.24
L_{MM}-4	12.4	1.11
D_{MM}-1	8.54	1.17
D_{MM}-2	10.5	1.15
D_{MM}-3	10.5	1.08
D_{MM}-4	16	1.05

Supplementary Figures

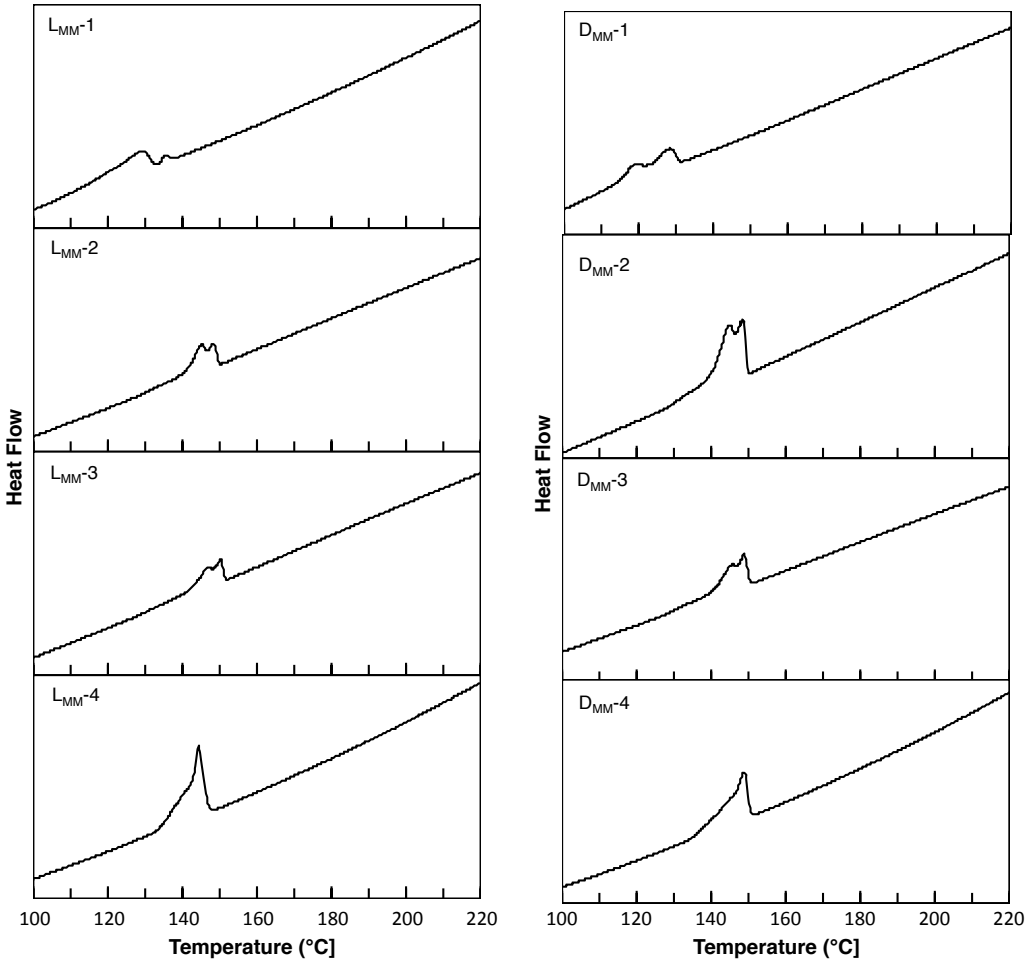


Figure 5-2. DSC traces of the pure macromonomers.

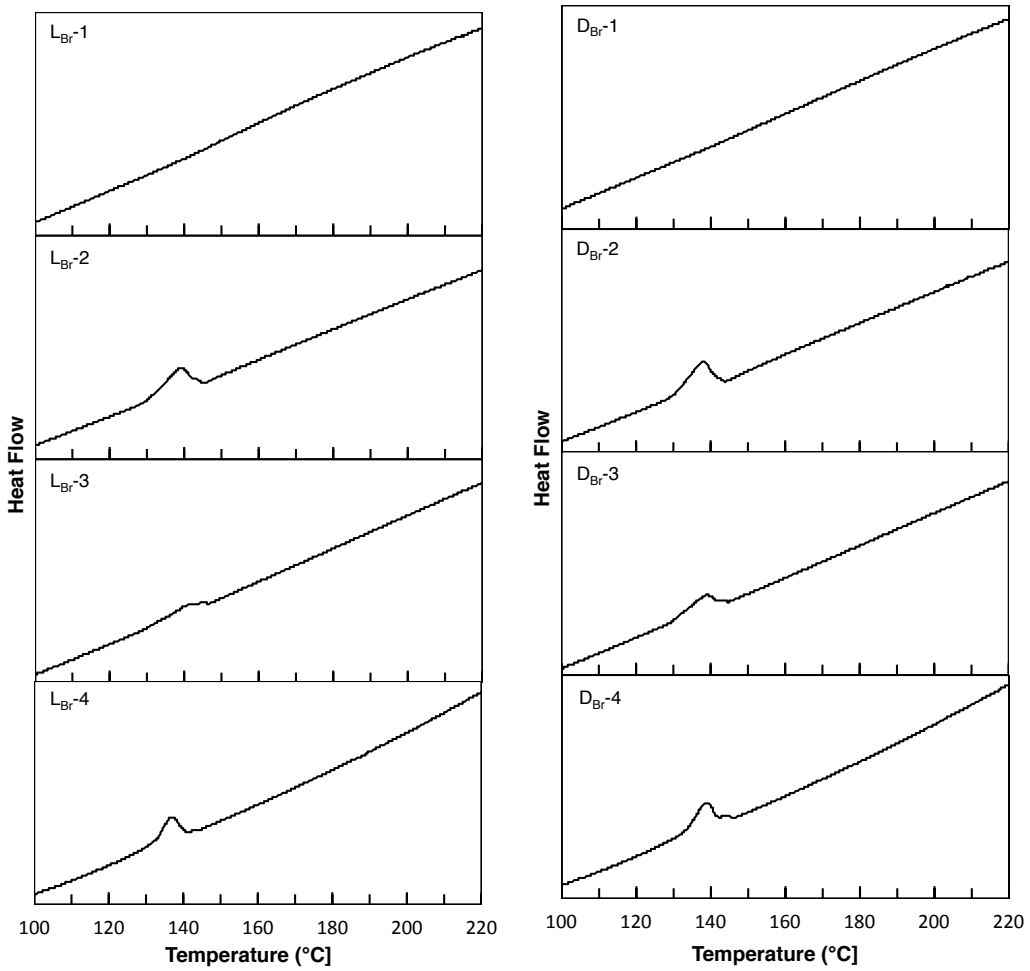


Figure 5-3. DSC traces of the pure brush copolymers.

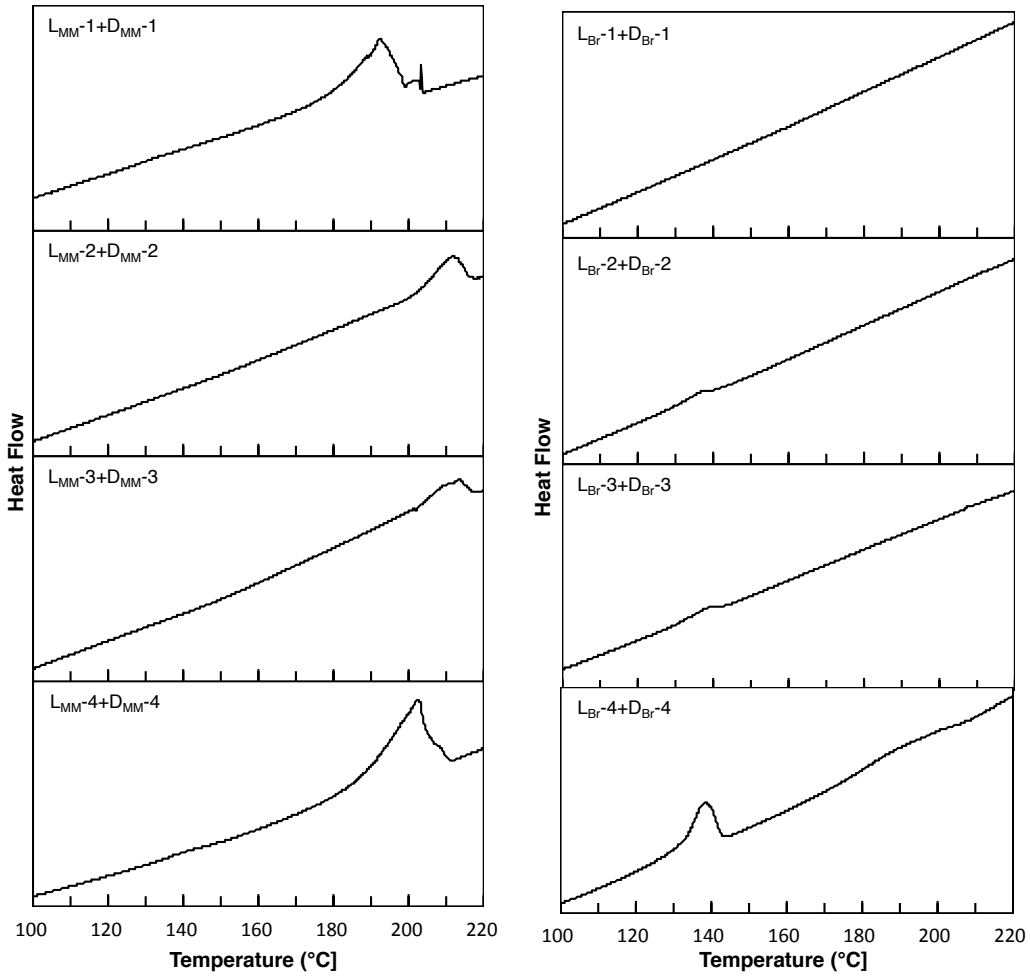


Figure 5-4. DSC traces of the MM/MM blends (left) and the brush/brush blends (right)

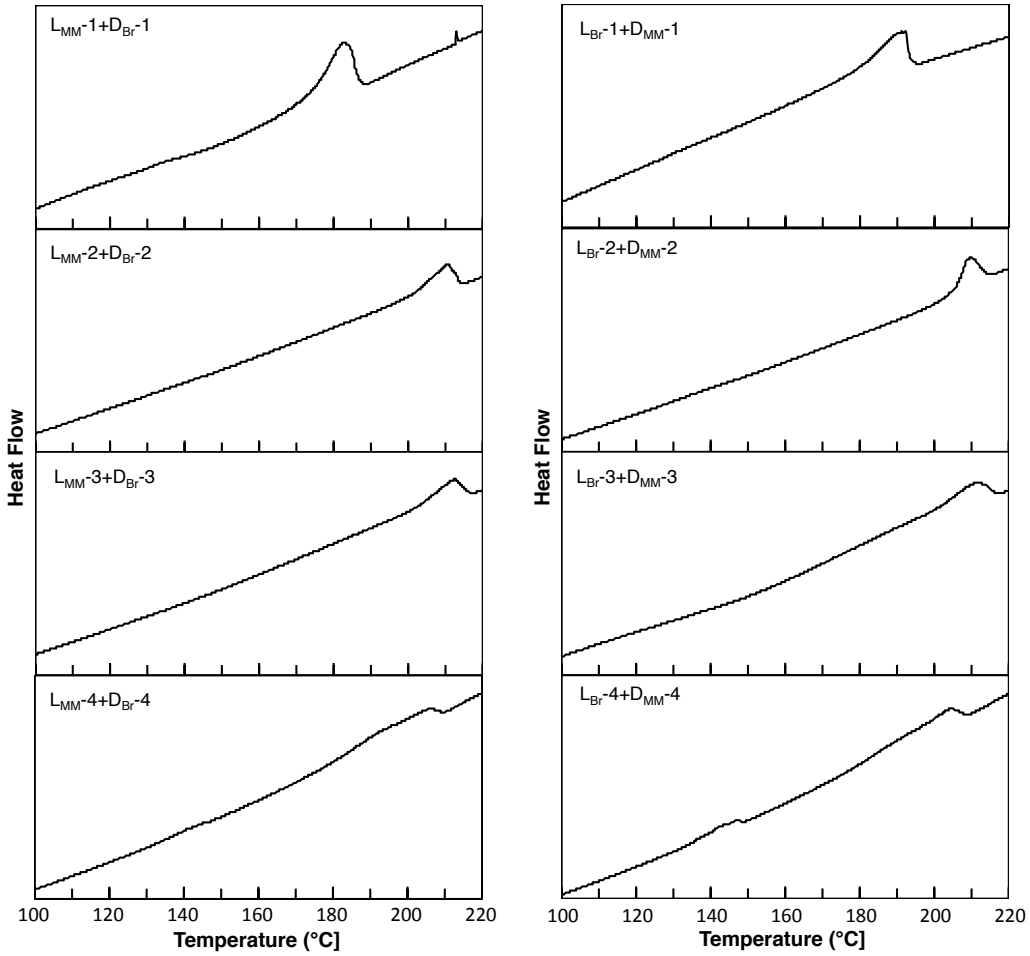


Figure 5-5. DSC traces of the MM/brush blends.

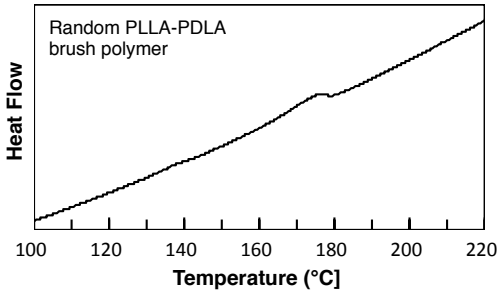


Figure 5-6. DSC trace of the random PLLA-PDLA brush copolymer.

REFERENCES

(1) Hu, M.; Xia, Y.; McKenna, G. B.; Kornfield, J. A.; Grubbs, R. H. *Macromolecules* **2011**, *44*, 6935–6943.

(2) Xia, Y.; Li, Y.; Burts, A. O.; Ottaviani, M. F.; Tirrell, D. A.; Johnson, J. A.; Turro, N. J.; Grubbs, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 19953–19959.

(3) Ikada, Y.; Jamshidi, K.; Tsuji, H.; Hyon, S.-H. *Macromolecules* **1987**, *20*, 904–906.

(4) Tsuji, H. *Macromol. Biosci.* **2005**, *5*, 569–597.

(5) Shin, E. J.; Jones, A. E.; Waymouth, R. M. *Macromolecules* **2012**, *45*, 595–598.

(6) Tsuji, H.; Hyon, S.-H.; Ikada, Y. *Macromolecules* **1991**, *24*, 5651–5656.

(7) Tsuji, H.; Ikada, Y.; Hyon, S.-H.; Kimura, Y.; Kitao, T. *J. Appl. Polym. Sci.* **1994**, *51*, 337–344.

(8) Takasaki, M.; Ito, H.; Kikutani, T. *J. Macromol. Sci., Part B Phys.* **2003**, *B42*, 403.

(9) Li, S.; Vert, M. *Macromolecules* **2003**, *36*, 8008–8014.

(10) Li, S. *Macromol. Biosci.* **2003**, *3*, 657–661.

(11) Schmidt, S. C.; Hillmyer, M. A. *J. Polym. Sci., Part B Polym. Phys.* **2001**, *39*, 300–313.

(12) Yamane, H.; Sasai, K. *Polymer* **2003**, *44*, 2569–2575.

(13) Fukushima, K.; Pratt, R. C.; Nederberg, F.; Tan, J. P. K.; Yang, Y. Y.; Waymouth, R. M.; Hedrick, J. L. *Biomacromolecules* **2008**, *9*, 3051–3056.

(14) Van Nostrum, C. F.; Veldhuis, T. F. J.; Bos, G. W.; Hennink, W. E. *Macromolecules* **2004**, *37*, 2113–2118.

(15) Hadjichristidis, N.; Pitsikalis, M.; Pispas, S.; Iatrou, H. *Chem. Rev.* **2001**, *101*, 3747–3792.

(16) Neiser, M. W.; Okuda, J.; Schmidt, M. *Macromolecules* **2003**, *36*, 5437–5439.

(17) Rizmi, A. C. M.; Khosravi, E.; Feast, W. J.; Mohsin, M. A.; Johnson, A. F. *Polymer* **1998**, *39*, 6605–6610.

(18) Heroguez, V.; Breunig, S.; Gnanou, Y.; Fontanille, M. *Macromolecules* **1996**, *29*, 4459–4464.

(19) Nyce, G. W.; Glauser, T.; Connor, E. F.; Möck, A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc* **2003**, *125*, 3046–3056.

(20) Csihony, S.; Culkin, D. A.; Sentman, A. C.; Dove, A. P.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc* **2005**, *127*, 9079–9084.

(21) Chabot, F.; Vert, M.; Chapelle, S.; Granger, P. *Polymer* **1983**, *24*, 53–59.

(22) Miyake, G. M.; Chen, E. Y. *Macromolecules* **2011**, *44*, 4116–4124.

(23) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2002**, *41*, 4035–4037.

(24) Matson, J. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **2008**, *130*, 6731–6733.